#### Remarks

Claims 2-14 are pending in the present application. Claims 12-15, as filed in the original application, were renumbered by Preliminary Amendment to read as claims 11-14.

Claims 1-5, 7, and 11-14 have been canceled herein without prejudice. Independent claim 6 has been amended by incorporating the element "wherein the G12 protein α-subunit mutant comprises the Q229L mutation" from its former dependent claim, canceled claim 7. Support for amended claim 6 is found throughout the specification as filed, particularly at canceled claim 7, and also at page 8, line 2 to line 25, FIG. 2A, FIG. 3, and FIG. 5. Claims 8, 9, and 10 have been amended to recite their dependence from amended claim 6, instead of canceled claim 7. Support for this amendment to claims 8, 9, and 10 is found in amended claim 6 and in canceled claim 7.

## **Drawing Compliance**

The Examiner has objected to Figure 4 as failing to comply with 37 CFR 1.84(p)(5). The Examiner asserts that the figure description fails to explain the association of the "+" and "-" labels with the bars in the graph. The figure description has been amended to describe the association of the "+" and "-" labels on the abscissa of the bar graph with the bars representing the various groups. The "+" label indicates groups treated with 10  $\mu$ M COX-2 inhibitor, while the "-" label indicates the groups which were not treated with COX-2 inhibitor. Support for this amendment is found in the original description of Figure 4, Figure 4, and in Example 2 (page 18, line 22 to page 19, line 18).

### Response to 35 U.S.C. § 112, second paragraph, indefiniteness rejection

Claims 2-5 and 11-14 again stand rejected as allegedly indefinite. Although not necessarily agreeing with the reasoning of the Examiner, claims 2-5 and 11-14 have been canceled herein, therefore the rejection as to these claims is moot.

# Response to 35 U.S.C. § 112, first paragraph, enablement rejection

Independent claims 2, 6, and 11 stand rejected as allegedly lacking enablement. The Examiner asserts at page 5 of the Office Action that the specification is enabling for a method of determining a test substance as a COX-2 inhibitory agent, wherein COX-2 is induced in an indicator cell by the specific  $\alpha$ G12 mutant,  $\alpha$ G12QL. However, the Examiner

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again alleges that the specification does not reasonably provide enablement for such a method wherein COX-2 is induced in an indicator cell by any or all types of  $\alpha$ G12 mutants.

Claims 2 and 11 have been canceled herein, therefore the rejection as to these claims is moot.

Claim 6 encompasses a method for screening a test substance for COX-2 inhibitory activity, by determining the level of one or more prostaglandins produced by indicator cells expressing a GTPase-deficient mutant form of the  $\alpha$ -subunit of protein G12. Although not necessarily agreeing with the reasoning of the Examiner, as described above, claim 6 has been amended by incorporating the element "wherein the G12 protein  $\alpha$ -subunit mutant comprises the Q229L mutation" from cancelled claim 7. As admitted by the Examiner, the application is enabled for the specific  $\alpha$ G12 mutation,  $\alpha$ G12QL is referred to as "Q229L" in amended claim 6 and throughout the specification.

Amended claim 6 is now enabled because it recites the specific  $\alpha G12$  mutation, Q229L, and not other  $\alpha G12$  mutants. Applicants request that the rejection as to claim 6 be withdrawn and submit that claim 6 and its dependent claims, i.e., 8, 9, and 10, are in condition for allowance.

### Response to 35 U.S.C. § 112, first paragraph, written description rejection

Claims 2, 6, and 11 again stand rejected as allegedly lacking written description. The Examiner alleges at page 9 of the Office Action that the claims are directed to a method where a genus of modified polypeptide sequences of  $\alpha G12$  is used. The Examiner further alleges that no description for modified polypeptide sequences has been provided beyond the characterization of a single mutant, i.e.,  $\alpha G12QL$ . The Examiner further alleges that the specification does not contain any disclosure of the structure of all the modified  $\alpha G12$  polypeptide sequences capable of inducing COX-2 in indicator cells. The Examiner alleges that because only a single species of the claimed genus is disclosed, that one of skill in the art cannot reasonably conclude that Applicants had possession of the invention at the time the application was filed.

While not necessarily agreeing with the reasoning of the Examiner, claims 2 and 11 have been canceled herein, therefore, the rejection as to these claims is moot. Furthermore, as discussed above, claim 6 has been amended to incorporate the element "wherein the G12 protein  $\alpha$ -subunit mutant comprises the Q229L mutation" of canceled claim 7. Because

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amended claim 6 now recites only the single mutant  $\alpha G12QL$ , i.e., Q229L, claim 6 now satisfies the written description requirement. Applicants request that the rejection as to claim 6 be withdrawn and submit that claim 6 and its dependent claims, i.e., 8, 9, and 10, are in condition for allowance.

### Conclusion

Based on the foregoing, amended independent claim 6 and amended dependent claims 8, 9, and 10 are believed in condition for allowance. An early and favorable action toward that end is earnestly solicited.

Respectfully submitted,

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